Chronic idiopathic pulmonary fibrosis in a West Highland white terrier

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Abstract — A 9-year-old, spayed, female West Highland white terrier was presented with a chronic cough, lethargy, and exercise intolerance. Thoracic radiographic findings were consistent with a marked interstitial lung pattern. Idiopathic pulmonary fibrosis, a disease anecdotally linked to this breed, was diagnosed on postmortem examination.

Résumé — Fibrose pulmonaire idiopathique chronique chez un West Highland White terrier. Une femelle West Highland White terrier de 9 ans, stérilisée, a été présentée avec des symptômes de toux chronique, léthargie et intolérance à l'effort. Les résultats de radiographie thoracique étaient compatibles avec une importante condition pulmonaire interstitielle. La fibrose pulmonaire idiopathique, une maladie reliée de façon anecdotique à cette race, a été diagnostiquée à l'examen post-mortem.

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A 9-year-old, spayed, female West Highland white terrier was presented with a history of lethargy, exercise intolerance, and a productive cough of 2 mo duration. The clinical signs had progressed over this period. There was no history of travel, exposure to toxic agents, weight loss, or previous medications. Vaccinations were current, the dog had tested negative for heartworm and was on heartworm prophylaxis. On auscultation of the chest, generalized moderate inspiratory crackles and expiratory wheezes were noted. The cough could not be elicited on tracheal palpation. No cardiac murmur was detected, and no other abnormalities were noted on physical examination. Lateral and dorsoventral thoracic radiographs were taken, and a generalized marked interstitial pattern of the lungs was noted. A complete blood cell (CBC) count and serum biochemical profile, along with a bronchoalveolar lavage or lung biopsy, were recommended but declined by the owner. Differential diagnoses included chronic bronchitis, neoplasia, idiopathic pulmonary fibrosis (IPF), and infectious diseases. No treatment was instituted at this time.

Three mo after initial presentation, the exercise intolerance and cough had increased significantly in both severity and frequency. Physical examination revealed generalized, marked crackles and wheezes on thoracic auscultation, and an exaggerated inspiratory and expiratory effort. Thoracic radiographs were retaken and revealed a diffuse interstitial pattern of increased radiopacity in the lung field. Hematologic and serum biochemical parameters were within normal reference ranges and a fecal Baermann test for lung worms was negative. A transtracheal wash was performed. Fifteen milliliters of sterile water were infused through a polypropylene catheter passed down a sterile endotracheal tube and approximately 5 mL of fluid was aspirated. Cytologic examination of the aspirated fluid revealed numerous cells on a thick, mucoid background. A majority of the cells were well-preserved neutrophils and no bacteria were present. A significant number of eosinophils, up to 10% in 1 smear and a small number of alveolar macrophages and well-differentiated epithelial cells were also present. Culture and sensitivity testing of the aspirated fluid indicated the presence of a moderate number of *Staphylococcus aureus* organisms, which were attributed to oral contamination. The results of the transtracheal wash were suggestive of active inflammation without a known etiology. A working diagnosis of chronic interstitial disease or idiopathic pulmonary fibrosis was made. Since a definitive diagnosis had not been obtained and the transtracheal wash might not have been representative of smaller airway disease, the patient was prescribed theophylline (Theo-Dur; Astra Pharma, Mississauga, Ontario), 10 mg/kg body weight (BW), PO, q8h, for 7 d, and enrofloxacin (Baytril; Bayer, Toronto, Ontario), 5 mg/kg BW, PO, q12h, for 14 d. An immunosuppressive dose of dexamethasone (Dextab; Vétoquinol, Lavaltrie, Quebec) was also prescribed, beginning at 0.5 mg/kg BW, PO, q12h, with the dosage declining over a period of 15 d, at which time it was terminated. A mild improvement was noted 2 wk after treatment was initiated.

The animal returned 10 mo after the initial presenting complaint, because its clinical condition had deteriorated. On physical examination, severe generalized crackles and wheezes were detected on thoracic auscultation, and a marked inspiratory and expiratory effort was

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observed. The animal was euthanized and a necropsy was performed. Histologic examination of several lung samples indicated generalized alveolar fibrosis and mineralization. In less mineralized areas where the fibrosis could be studied more closely, perivascular hyalinization was noted. Bronchioles appeared normal. The histopathologic diagnosis was IPF.

Idiopathic pulmonary fibrosis is a disease that affects the lower respiratory tract in older animals and results in breathing abnormalities and exercise intolerance. Since clinical signs are not usually detected until substantial and irreversible pulmonary damage has compromised gas exchange mechanisms, treatment is palliative to optimize the quality of life (1,2). Anecdotally, an abnormally high number of cases have been noted in older West Highland white terriers; however, to date a breed predisposition has not been confirmed (1–7). Recently, it has been suggested that other terrier breeds may experience this disease process, including the Jack Russell terrier, the Staffordshire bull terrier and the Cairn terrier (4,5,7).

Idiopathic pulmonary fibrosis is of unknown etiology, although infectious processes, drug reactions, exposure to toxins or dusts, and connective tissue disorders have been hypothesized as possible causes of the disease (1,6–8). In humans, there is a correlation between a positive antinuclear antibody (ANA) titer and IPF (7). This suggests the possibility of an immune-mediated cause of pulmonary fibrosis. Currently, this link has not been shown in dogs (7), although ANA titers are seldom determined in dogs presenting with chronic pulmonary disorders. Although the initiating factor or factors of IPF are not known, the progression of the disease is better understood. Chronic alveolitis develops slowly over a period of months to years, reducing gas exchange across the alveolar wall and the surrounding capillary bed (2). At some point, injury to the alveolar wall becomes irreversible and fibrosis of the alveolar wall begins (2,6). This fibrosis results in an increase in the density of interstitial lung tissue (1). Secondary mineralization of the pulmonary parenchyma may follow this initial fibrosis.

Clinical presentation of IPF usually includes a long and progressive history of dyspnea, with or without the presence of a cough (2–4,7). Auscultation demonstrates ventral end-inspiratory and early-expiratory crackles that are bilateral and are most evident on full inspiration (1,2). As in this case, exercise intolerance is a feature of the condition. In severely affected animals, minor exertion will result in tachypnea, open-mouthed breathing, and cyanosis (1,2).

Differentiating IPF from other chronic pulmonary disorders can be challenging, especially since interstitial lung diseases in the dog are poorly understood (4,5,7). There are several diagnostic tools that should be utilized. Radiographic patterns associated with IPF are characteristic of generalized interstitial disease and serve as a good starting point in the diagnostic process (3–6). Generally, in IPF, bronchoscopic evaluation of the respiratory tract will reveal normal respiratory structures, and this method can rule out disorders such as chronic bronchitis (4,5). On cytologic examination, bronchoalveolar lavage fluid from an animal with IPF should either appear normal or indicate a mild nonseptic process (4). This contrasts markedly from abnormal findings in a case of pulmonary infection or neoplasia. The best antemortem diagnostic test for IPF is pulmonary biopsy (7). Pulmonary changes associated with this disorder include moderate to severe alveolar fibrosis and mineralization, and alveolar epithelialization (2–4). There may or may not be bronchiolar involvement (7). These findings should rule out all previously suggested differential diagnoses. Typically, at necropsy, the lungs do not completely collapse when the thoracic cavity is opened (7). The lungs may appear pale and have areas of consolidation (7). Histologic examination of pulmonary samples collected at necropsy should be diagnostic in cases of IPF.

Several differential diagnoses must be considered along with IPF. Chronic bronchitis is a disease that is recognized in terrier breeds and a long-standing case may mimic a case of IPF (4,5). Generally, on thoracic radiographs, a dog with chronic bronchitis will have increased bronchial markings, although these may be seen with IPF (4,5). Chronic mucosal changes; such as hyperemia, edema, and an irregular or mottled surface, should be evident on bronchoscopic examination (4). Cardiogenic and noncardiogenic edema can be differentiated from IPF by using the history, physical examination, and thoracic radiography (4,5). Bacterial and fungal processes can be ruled out with the use of a CBC count, serum biochemical analysis, urinalysis, cytologic examination, and culture and sensitivity testing of a bronchoalveolar lavage (4). Parasitism can be assessed by performing a Baermann test to rule out lung worm infestation (4). Infiltrative neoplasia can be ruled out with a bronchoalveolar lavage, a lung biopsy, or both, if necessary. The duration of clinical signs will rule out paraquat poisoning or other acute lung damage, as IPF usually follows a long and slowly progressive history of respiratory difficulty (2,4). Since IPF occurs in older animals, there are often other concurrent disorders that can confound the diagnosis. For example, a similar radiographic appearance may be seen in animals suffering from hyperadrenocorticism (4,5).

The mean age of onset of IPF is 9 y, and life expectancy is approximately 18 mo after the onset of clinical signs, or approximately 11 mo following diagnosis (4). The symptomatic treatment of IPF involves the use of corticosteriods, bronchodilators, and, when necessary, oxygen therapy (1). Some patients may require immunosuppressive doses of corticosteroids. Recently, the use of antifibrotic agents and immune modulators in humans was reviewed (9). Although to date there is minimal data, initial studies suggest that some of the therapeutics show promise in reducing the fibrosis associated with IPF (9).

Current methods of diagnosis generally do not allow for early detection of IPF; awareness of its occurrence in West Highland white terriers and other terrier breeds should raise one's index of suspicion when a dog of these breeds is presented with the associated clinical signs. More research is required to determine if a real correlation exists between certain terrier breeds and IPF. Also, more information on IPF is needed to improve early diagnostic techniques and provide a

treatment that can be initiated before permanent damage occurs to the pulmonary parenchyma. Once the etiology or etiologies of IPF are better understood, it will be possible to determine if there is a genetic or familial component to the development of this disease.

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Answers to Quiz Corner/Les réponses du test éclair

1. b — Lagomorphs possess atropinase, which quickly lyses atropine, rendering it ineffective.
   b — Les lagomorphes élaborent l'atropinase qui lyse rapidement l'atropine, la rendant inefficace.

2. e — Birds should be treated for psittacosis for at least 45 days.
   e — Les oiseaux devraient être traités pour la psittacose durant au moins 45 jours.

3. a — Cats ingest *Toxoplasma* cysts found in muscles (raw meat) of rodents and other meat sources.
   a — Les chats ingèrent les kystes de Toxoplasma *retrouvés dans les muscles (viande crue) des rongeurs et de d'autres sources de viande.*

4. c — Campylobacteriosis is an acute enteritis of dogs that is transmissible to people. Salmonellosis is possible but unlikely. Giardiosis would probably not cause bloody diarrhea. Yersiniosis is very rare in dogs.
   c — La campylobactériose est une entérite aiguë des chiens qui est transmissible aux humains. La salmonellose est possible mais peu probable. La giardiose ne causerait probablement pas de diarrhée sanglante. La yersiniose est très rare chez les chiens.

5. c — Enamel hypoplasia is caused by an insult during tooth development. Vitamin C supplementation should cause no insult.
   c — L'hypoplasie de l'émail est causée par un désordre au cours du développement des dents. Un supplément de vitamine C ne devrait pas causer de problème.

6. d — Joint immobilization leads to joint contracture, muscle atrophy, and other aspects of "fracture disease."
   d — L'immobilisation des articulations conduit à la contracture articulaire, à l'atrophie musculaire et à d'autres aspects des maladies associées aux fractures.

7. c — The slap (adductor reflex) test is not a reliable test for laryngeal hemiplegia.
   c — Le test du réflexe des adducteurs n'est pas fiable pour l'hémiplégie laryngée.

8. b — The testicles have normally migrated into the scrotum by the beginning of the 5th month of gestation in bovine fetuses.
   b — Chez les bovins, les testicules descendent normalement dans le scrotum du fœtus au début du cinquième mois de gestation.

9. a — Carrier ewes harbor *Campylobacter* organisms in the gastrointestinal tract and contaminate the premises, allowing oral infection of susceptible ewes.
   a — Les brebis porteuses possèdent du Camphylobacter *dans leur tractus gastro-intestinal et contaminent ainsi l'environnement, permettant l'infection orale des brebis sensibles.*

10. c — Interdigital hyperplasia can produce progressive lameness. Once the lesion has increased to several centimeters in size and produces pain, resection is the only reliable method of treatment. Smaller, nonpainful lesions may be managed in the short term with topical antiseptic therapy.
    c — L'hyperplasie interdigitée peut causer une boiterie progressive. Lorsque la lésion atteint une grosseur de plusieurs centimètres et cause de la douleur, l'ablation est le seul traitement valable. De petites lésions non douloureuses peuvent être traitées à court terme par des antiseptiques topiques.